09-15-00 A

Attorney Docket No.: 6028.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

FILING UNDER 37 C.F.R. 1.53(b)

Box Patent Application
Assistant Commissioner for Patents
Washington, DC 20231

Express Mail Label No. EL636737496US
Date of Deposit September 14, 2000

Sir:

This is a request for filing a patent application under 37 C.F.R. 1.53(b) of

Applicant(s): Tina Meinertz Andersen

Title: Composition Containing a Meiosis Activating Substance

11 pages of specification 3 sheets of Declaration and Power of Attorney

[x] The filing fee is calculated as follows:

Basic Fee:	$690.00
Total Claims: 19 - 20 = 0 x 18 =	$0
Independent Claims: 1 - 3 = 0 x 78 =	$0
Total Fee:	$690.00

Address all future communications to Steve T. Zelson, Esq., Novo Nordisk of North America, Inc., 405 Lexington Avenue, Suite 6400, New York, NY 10174-6401.

Please charge the required fee, estimated to be $690, to Novo Nordisk of North America, Inc., Deposit Account No. 14-1447. A duplicate of this sheet is enclosed.

Respectfully submitted,

Date: September 14, 2000

Valeta A. Gregg

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Attorney Docket No.: 6028.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

EXPRESS MAIL CERTIFICATE

Box Patent Application
Assistant Commissioner for Patents
Washington, DC 20231

Re: U.S. Patent Application for
Title: Composition Containing a Meiosis Activating Substance
Applicants: Tina Meinertz Andersen

Sir:

Express Mail Label No. EL636737496US

Date of Deposit : September 14, 2000

I hereby certify that the following attached paper(s) or fee

1. Filing Under 37 C.F.R. 1.53(b) (in duplicate)
2. Patent Application
3. Unexecuted Combined Declaration and Power of Attorney
4. Preliminary Amendment

are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" under 37 C.F.R. 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, DC 20231.

Miriam Kelly
(Name of person mailing paper(s) or fee)

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Attorney Docket No.: 6028.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Tina Meinertz Andersen

Application No.: TBA Group Art Unit: TBA

Filed: September 13, 2000 Examiner: TBA

For: Composition Containing a Meiosis Activating Substance

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Before the above-captioned application is taken up for examination, entry of the following amendment is respectfully requested:

IN THE CLAIMS:

Please cancel claim 13, and amend the claims as follows:

1. (Amended) A solid composition, comprising meiosis activating substance [product containing] (MAS) and an additive.

2. (Amended) [A] The composition[, according to Claim] of claim 1, [characterized in that the content of water therein is] wherein the composition comprises a water content of below 10%[, preferably below 5%, more preferred below 1%] (weight/weight).

3. (Amended) [A composition, according to any one of the preceding claims] The composition of claim 1, [characterised in that the content of] wherein the composition

comprises an organic solvent [therein is] content below 10 %[, preferably below 5%, more preferred below 1%] (weight/weight).

4. (Amended) [A composition, according to any one of the preceding claims, characterised in that the content of] The composition of claim 1, wherein the composition comprises a MAS [therein is] content below 50%[, preferably below 20%, more preferred below 10%, most preferred below 5%] (weight/weight).

5. (Amended) [A composition, according to any one of the preceding claims, characterised in that the] The composition of claim 1, wherein MAS is selected from the group comprising 4,4-dimethyl-5α-cholesta-8,14,24-triene-3β-ol; 4,4-dimethyl-5 -cholest-8,14,24-trien-3 -ol hemisuccinate; 5 -cholest-8,14-dien-3 -ol; 5 -cholest-8,14-dien-3 -ol hemisuccinate; (20S)-cholest-5-en-3 ,20-diol; 3 -hydroxy-4,4-dimethyl-5 -chola-8,14-dien-24-oic acid-N-(methionine) amide; and cholest-5-en-16 -ol.

6. (Amended) [A composition, according to any one of the preceding claims, characterised in that] The composition of claim 1, wherein the additive is a protein or a phosperglycid.

7. (Amended) [A composition, according to any one of the preceding claims, characterised in that it can be used for preparing an] An aqueous solution comprising the composition of claim 1 [with the characteristics mentioned in any of the following claims].

8. (Amended) [A composition, according to any one of the preceding claims, characterised in that it can be used for preparing an] The aqueous solution of claim 7, wherein [which when used for the] treatment of oocytes with the aqueous solution results in a percentage germinal vehicle breakdown (GVB) of at least 50%,[preferably at least 80%,] when MAS is FF-MAS.

9. (Amended) [An aqueous solution of MAS, characterised in that] The aqueous solution of claim 7, wherein the content of MAS is at least 0.001 μg/ml[, preferably at least 0.01 μg/ml, more preferred at least 0.1 μg/ml, even more preferred at least 0.5 μg/ml].

10. (Amended) [An aqueous solution of MAS, according to the preceding claim, characterised in that] The aqueous solution of claim 9, wherein the content of MAS is not more than 0.1 g/ml[, preferably not more than 0.01 g/ml].

11. (Amended) [An] The aqueous solution [of MAS according to any one of the two preceding claim, characterised in that the content of] of claim 7, comprising an organic solvent content [is] of less than 0.1%[, preferably less than 0.05%, most preferred less than 0.01%].

12. (Amended) A device [having] comprising a hollow containing [a solid product or a solution according to any of the previous claims] the composition of claim 1.

Please add the following new claims:

14. (New) The composition of claim 2, wherein the water content is below 5%.

15. (New) The composition of claim 14, wherein the water content is below 1%.

16. (New) The composition of claim 3, wherein the organic solvent content is below 5%.

17. (New) The composition of claim 16, wherein the organic solvent content is below 1%.

18. (New) The composition of claim 4, wherein the MAS content is below 20%.

19. (New) The composition of claim 18, wherein the MAS content is below 10%.

20. (New) The composition of claim 19, wherein the MAS content is below 5%.

REMARKS

Claim 13 is cancelled. New claims 14-20 are added. Therefore, claims 1-12 and 14-20 are pending. This amendment is submitted to correct improper multiple dependent

claims and to conform the claims to US practice. Subject matter cancelled from the claims is presented as new claims 14-20. Since only dependencies are altered, there is no new matter added, and entry of the amendment is respectfully requested.

Respectfully submitted,

Date: 14 September 2000

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FIELD OF THIS INVENTION

The present invention relates to a solid product which can be used in connection with *in vitro* fertilisation.

BACKGROUND OF THIS INVENTION

Several meiosis activation substances (hereinafter designated MAS) have been found. When MAS are kept in a medium containing oocytes, the oocytes becomes more prone to become fertilised. However, a major problem with the use of MAS is that, usually, they have a very low solubility.

SUMMARY OF THIS INVENTION

One object of this invention is to develop a composition containing MAS or a derivative thereof which can be dissolved in an aqueous medium.

Another object is to develop a composition containing MAS or a derivative thereof which can be dissolved in an aqueous medium without any physical influence such as heating, stirring, or ultrasound treatment.

DETAILED DESCRIPTION OF THIS INVENTION

The solubility of a preferred MAS, i.e., FF-MAS, in water is very low, i.e., approximately 20 picogram/ml (corresponding to 2×10^{-5} μg/ml) , and in ethanol the solubility is substantially higher, i.e., approximately 4 mg/ml. According to our preliminary investigations, the highest solubility of FF-MAS in a mixture of ethanol and water (1:2.5) is approximately 0.4 mg/ml. Several other MAS have a similar low solubility in water.

Surprisingly, it has now been found that a solid composition containing MAS and an additive have a good solubility in water. The additives are components which, when added to MAS, provides a composition which can be used to prepare an aqueous solution containing MAS.

Examples of additives are water soluble proteins such as serum albumin, e.g. human serum albumin (hereinafter designated HSA), optionally in recombinant form, enzymes and phospherglycerider such as phosphatidylethanolamin, phosphatidylcholine, phosphatidylserine, phosphatidylnositol.

Preferably, the compositions of this invention have a content of water below 10 %, preferably below 5%, more preferred below 1% (weight/weight).

Preferably, the compositions of this invention have a content of organic solvent below 10 %, preferably below 5%, more preferred below 1% (weight/weight).

Preferably, the compositions of this invention have a content of MAS below 1%, preferably below 0.1%, more preferred below 0.05% (weight/weight).

Preferably, the compositions of this invention have a content of additive higher than 99%, more preferred higher than 99.9%.

Preferred compositions of this invention are such which can be treated with an aqueous medium containing no or only low concentrations of organic solvent result in a solution containing MAS. Preferably, these aqueous media contain less than 1%, preferably less than 0.5%, more preferred less than 0.1% of organic solvent (weight/weight).

Earlier, several attempts to prepare compositions fulfilling this requirement have failed.

Herein, the term MAS designates compounds which mediate the meiosis of oocytes. More specifically, MASs are compounds which in the test described in Example 1 below has a percentage germinal vesicle breakdown (hereinafter designated GVB) which is significantly higher than the control. Preferred MAS are such having a percentage GVB of at least 50%, preferably at least 80%. Examples of preferred MASs are 4,4-dimethyl-5α-cholesta-8,14,24-triene-3β-ol (hereinafter designated FF-MAS); 4,4-dimethyl-5α-cholest-8,14,24-trien-3β-ol hemisuccinate; 5α-cholest-8,14-dien-3β-ol; 5α-cholest-8,14-dien-3β-ol hemisuccinate; (20S)-cholest-5-en-3β,20-diol; 3β-hydroxy-4,4-dimethyl-5α-chola-8,14-dien-24-oic acid-N-(methionine) amide; and cholest-5-en-16β-ol. Further examples of MASs are mentioned in WO 96/00235, 96/27658, 97/00884, 98/28323, 98/54965 and 98/55498, more specifically in Claim 1 thereof.

One way of preparing the compositions of this invention is to mix a solution of MAS in an organic solvent such as ethanol with an aqueous solution of the additive and, thereafter to wait

until the solvent is evaporated. The evaporation can be accelerated by using continuous air-flow over the product, vacuum, or any other feasible methods to remove the solvent. The product marketed could be a delivery system having one or more depressions or hollows. Hereinafter, these depressions and hollows are mutually designated hollows. At least one of these hollows contain a composition according to this invention. A convenient way of placing the solid MAS therein is first to place a solution containing MAS and the additive in the hollow and thereafter to evaporate the solution. In this way, the evaporation residue, i.e., the composition according to this invention, is placed directly in the hollow in said device (delivery system).

Since the composition of this invention is to be used for the treatment of oocytes, it is important that the composition of this invention does not contain constituents which influence the oocytes negatively.

One way of using the compositions of this invention is to dissolve the composition in an aqueous medium such as water and then, if desired, to add other constituents which may have a favourable influence on the maturation of the oocytes.

Another way of using the composition is to dissolved it in a media normally used for in vitro maturation.

The present invention is further illustrated by the following examples which, however, are not to be construed as limiting the scope of protection. The features disclosed in the foregoing description and in the following examples may, in any combination thereof, be material for realising the invention in diverse forms thereof.

Example 1

Method used for determining whether a compound is a MAS or not.

Oocytes were obtained from immature female mice (C57BL/6J x DBA/2J F1, Bomholtgaard, Denmark) weighing 13-16 grams, that were kept under controlled temperature (20-22 °C), light (lights on 06.00-18.00) and relative humidity (50-70%). The mice received an intraperitoneal injection of 0.2 ml gonadotropins (Gonal-F, Serono) containing 20 IU FSH and 48

hours later the animals were killed by cervical dislocation. The ovaries were dissected out and the oocytes were isolated in Hx-medium (see below) under a stereo microscope by manual rupture of the follicles using a pair of 27 gauge needles. Spherical oocytes displaying an intact germinal vesicle (hereinafter designated GV) were divided in cumulus enclosed oocytes (hereinafter designated CEO) and naked oocytes (hereinafter designated NO) and placed in α-minimum essential medium (α-MEM without ribonucleosides, Gibco BRL, Cat. No. 22561) supplemented with 3 mg/ml bovine serum albumin (BSA, Sigma Cat. No. A-7030), 5 mg/ml human serum albumin (HSA, State Serum Institute, Denmark), 0.23mM pyruvate (Sigma, Cat. No S-8636), 2 mM glutamine (Flow Cat. No. 16-801), 100 IU/ml penicillin and 100 μg/ml streptomycin (Flow, Cat No. 16-700). This medium was supplemented with 3 mM hypoxanthine (Sigma Cat. No. H-9377) and designated Hx-medium.

The oocytes were rinsed three times in Hx-medium and oocytes of uniform size were divided into groups of CEO and NO. CEO and NO were cultured in 4-well multidishes (Nunclon, Denmark) in which each well contained 0.4 ml of Hx-medium and the compound to be tested in a concentration of 10 μM. One control well (i.e., 35-45 oocytes cultured in identical medium with no addition of test compound) was always cultured simultaneously with 3 test wells (35-45 oocytes per well supplemented with test compound).

The oocytes were cultured in a humidified atmosphere of 5% CO_2 in air for 24 hours at 37°C. By the end of the culture period, the number of oocytes with GV, GVB and polar bodies (hereinafter designated PB), respectively, were counted using a stereo microscope (Wildt, Leica MZ 12). The percentage of GVB, defined as percentage of oocytes undergoing GVB per total number of oocytes in that well, was calculated as:

% GVB = ((number of GVB + number of PB)/ total number of oocytes) X 100.

Example 2

Method used for determining whether a compound can be used as the additive in the compositions of this invention or not.

An additive for FF-MAS compositions are characterised by :

Improving the solubility of FF-MAS in ethanol/water (1:2.5 v/v)

Ensuring a clear solution of FF-MAS after reconstitution of the composition in MEM Alpha Medium.

Securing percent GVB is at least 50% preferable 80% when tested on oocytes obtained from immature female mice.

Prepare a saturated ethanolic solution of FF-MAS. Blend with an aqueous solution of the additive in the ration 1:2,5. By visual inspection control that surplus FF-MAS is available in the solution. Rotate the solution for 24 hours at room temperature. Filter the solution through 0,22μm filter, determine the content of FF-MAS by HPLC and calculate the solubility. Transfer 350μl to 4-well dish and evaporate to dryness at room temperature. Add 500μl MEM ALPHA medium (Gibcobal). If a clear solution is obtained within half an hour, the composition is tested on oocytes obtained from immature female mice. % GVB obtained is at least 50%, preferable 80%, *vide* example 1.

Example 3

Composition containing Human Serum Albumin (HSA).

In this example, 3 products were prepared. Referring to the table below, the stock solution of FF-MAS used for product 1, 2, and 3 contained 50, 500 and 3330 μg/ml, respectively. For each of the products, the stock solution of HSA contained 20% HSA. The amount of said stock solutions used is stated in the table. For example, for product 1, 400 μl of the FF-MAS stock solution was mixed with 1000 μl of the HSA stock solution. After mixing of these stock solutions, the solutions were clear, and no precipitation was observed therein. After mixing, the amount thereof stated in the table was transferred to 4-well multi-dishes (Nuclon, Denmark). For example, for product 1, 350 μl of the mixture was transferred to the multi-dish Finally, the solutions were evaporated to dryness at room temperature. After evaporation, some of he products appears as an opalescent, clear film in the dishes, other are invisible to the human eye. The highest concentration of FF-MAS dissolved in this example is 0.95 mg/ml.

Before use, 500 μl MEM ALPHA Medium (Gibcobal) is added, and a clear solution of FF-MAS and HSA is obtained within half an hour at room temperature.

	4-well-multi dish No. 1	4-well-multi dish No. 2	4-well-multi dish No. 3
FF-MAS solution in ethanol, 50 µg/ml	400 µl	-	-
FF-MAS solution in ethanol, 500 µg/ml	-	400 µl	-
FF-MAS solution in ethanol, 3.33 mg/ml	-	-	450 µl
HSA solution in water, 20%	1000 µl	1000 µl	1125 µl
Amount transferred to multi-dish	350 µl	350 µl	525 µl
Ratio between FF-MAS and HSA	1 : 10,000	1 : 1,000	1 : 150
Appearance of solutions before evaporation	clear, colourless solutions, without precipitation		

Example 4

Compositions containing Human Serum Albumin (HSA).

Analogously as described in the previous example, solutions of FF-MAS in water/ethanol containing HSA were prepared in the concentrations stated below by sample mixing at room temperature. After preparation, the solutions were clear, and no precipitation was observed. The solutions were transferred to 4-well multi-dishes (Nuclon, Denmark). Finally, the solutions were evaporated to dryness at room temperature.

Before use, 500 µl MEM ALPHA Medium (Gibcobal) is added, and within half an hour at room temperature, a clear solution of FF-MAS and HSA is obtained.

The formulations were tested on oocytes obtained from immature female mice. % GVB for the respective formulation are stated in the table below.

	4-well-multi dish No. 1	4-well-multi dish No. 2	4-well-multi dish No. 3
FF-MAS solution in ethanol, 5.22 µg/ml	100 µl	-	-
FF-MAS solution in ethanol, 26.1 µg/ml	-	100 µl	-
FF-MAS solution in ethanol, 261 mg/ml	-	-	100 µl
HSA solution in water, 20%	250 µl	250 µl	250 µl
Ratio between FF-MAS and HSA	1 : 10,000	1 : 2,000	1 : 200
Theoretical quantity of FF-MAS per well	0.5 µg	2.5 µg	25 µg
% GVB	72	93	91

Example 5

Compositions containing Human Serum Albumin (HSA).

Analogously as described in the previous example, solutions of FF-MAS in water/ethanol containing HSA were prepared in the concentrations stated below by sample mixing at room temperature. After preparation, the solutions were clear, and no precipitation was observed. The solutions were transferred to 4-well multi-dishes (Nuclon, Denmark). Finally, the solutions were evaporated to dryness at room temperature.

Before use, 500 µl MEM ALPHA medium (Gibcobal) is added, and within half an hour at room temperature, a clear solution of FF-MAS and HSA is obtained.

The concentration of FF-MAS after reconstitution was determined by HPLC, and the results are stated below. The formulations were tested on oocytes obtained from immature female mice. %GVB for the respective formulations are stated below.

	4-well-multi-dish

	No. 1	No. 2	No. 3	No. 4	No. 5
FF-MAS solution in ethanol, 26.1 µg/ml	100 µl	-	-	-	-
FF-MAS solution in ethanol 7.83 µg/ml	-	100 µl	-	-	-
FF-MAS solution in ethanol, 5.22 mg/ml	-	-	100 µl	-	-
FF-MAS solution in ethanol, 2.5 µg/ml	-	-	-	100 µl	-
FF-MAS solution in ethanol, 0.5 µg/ml	-	-	-	-	100 µl
HSA solution in water, 20%	250 µl	250 µl	250 µl	250 µl	250 µl
Ratio between FF-MAS and HSA	1 : 100,000	1 : 20,000	1 : 10,000	1 : 6667	1 : 2000
Theoretical quantity of FF-MAS per well	0.05 µg	0.25 µg	0.5 µg	0.75 µg	2.5 µg
Percentage GVB	13	52	78	82	90

CLAIMS

1. A solid product containing MAS and an additive.

2. A composition, according to Claim 1, characterised in that the content of water therein is below 10 %, preferably below 5%, more preferred below 1% (weight/weight).

3. A composition, according to any one of the preceding claims, characterised in that the content of organic solvent therein is below 10 %, preferably below 5%, more preferred below 1% (weight/weight).

4. A composition, according to any one of the preceding claims, characterised in that the content of MAS therein is below 50%, preferably below 20%, more preferred below 10%, most preferred below 5% (weight/weight).

5. A composition, according to any one of the preceding claims, characterised in that the MAS is 4,4-dimethyl-5α-cholesta-8,14,24-triene-3β-ol; 4,4-dimethyl-5α-cholest-8,14,24-trien-3β-ol hemisuccinate; 5α-cholest-8,14-dien-3β-ol; 5α-cholest-8,14-dien-3β-ol hemisuccinate; (20S)-cholest-5-en-3β,20-diol; 3β-hydroxy-4,4-dimethyl-5α-chola-8,14-dien-24-oic acid-N-(methionine) amide; and cholest-5-en-16β-ol.

6. A composition, according to any one of the preceding claims, characterised in that the additive is a protein or a phosperglycid.

7. A composition, according to any one of the preceding claims, characterised in that it can be used for preparing an aqueous solution with the characteristics mentioned in any of the following claims.

8. A composition, according to any one of the preceding claims, characterised in that it can be used for preparing an aqueous solution which when used for the treatment of oocytes results in a percentage germinal vehicle breakdown (GVB) of at least 50%, preferably at least 80%, when MAS is FF-MAS.

9. An aqueous solution of MAS, characterised in that the content of MAS is at least 0.001 μg/ml, preferably at least 0.01 μg/ml, more preferred at least 0.1 μg/ml, even more preferred at least 0.5 μg/ml.

10. An aqueous solution of MAS, according to the preceding claim, characterised in that the content of MAS is not more than 0.1 g/ml, preferably not more than 0.01 g/ml.

11. An aqueous solution of MAS according to any one of the two preceding claim, characterised in that the content of organic solvent is less than 0.1%, preferably less than 0.05%, most preferred less than 0.01%.

12. A device having a hollow containing a solid product or a solution according to any of the previous claims.

13. Any novel feature or combination of features described herein.

Novo Nordisk A/S

ABSTRACT

A solid composition containing a meiosis activating substance can be prepared by adding a protein or a phosperglycid.

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (Includes Reference to PCT International Applications)	'Attorney's Docket Number: **6028.200-US**

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Composition Containing a Meiosis Activating Substance

The specification of which (check only one item below):
[ ] is attached hereto
[**X**] was filed as United States application

Application No. To Be Assigned

on September 14, 2000
and was amended
on

[ ] was filed as PCT international application
Number
on
and was amended under PCT Article 19
on

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by an amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability of this application in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim priority benefits under Title 35, United States Code, §119 of any provisional or foreign application(s) for patent or inventor's certificate or of any PCT international applications(s) for patent or inventor's certificate or of any PCT international applications(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR U.S. PROVISIONAL/FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY (if PCT, indicated "PCT")	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 USC 119
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY
(Includes Reference to PCT International Applications)

Attorney's Docket Number: **6028.200-US**

I hereby claim the benefit under Title 35, United States Code '120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this applications is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, '112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, '1 56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application

PRIOR U S APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U S FOR BENEFIT UNDER 35 U S C 120

U.S APPLICATIONS		STATUS (Check one)		
U S APPLICATION NUMBER	U S. FILING DATE	Patented	Pending	Abandoned

PCT APPLICATIONS DESIGNATING THE U.S

APPLICATION NO	FILING DATE	US SERIAL NUMBERS ASSIGNED (if any)			

POWER OF ATTORNEY As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith Steve T Zelson Elias J Lambiris Valeta A Gregg Carol E Rozek Robert L Starnes Reza Green, Reg No 30,335 Reg No 33,728 Reg No 35,127 Reg No 36,993 Reg No 41,324 Reg No 38,475

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1	Full Name of Inventor	**Family Name** **Andersen**	**First Given Name** **Tina**	**Second Given Name** **Meinertz**
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2	Full Name of Inventor	**Family Name**	**First Given Name**	**Second Given Name**
	Residence & Citizenship	**City**	**State or Foreign Country**	**Country of Citizenship**
	Post Office Address	**Post Office Address**	**City**	**State & Zip Code/Country**
3	Full Name of Inventor	**Family Name**	**First Given Name**	**Second Given Name**
	Residence & Citizenship	**City**	**State or Foreign Country**	**Country of Citizenship**
	Post Office Address	**Post Office Address**	**City**	**State & Zip Code/Country**
4	Full Name of Inventor	**Family Name**	**First Given Name**	**Second Given Name**
	Residence & Citizenship	**City**	**State or Foreign Country**	**Country of Citizenship**
	Post Office Address	**Post Office Address**	**City**	**State & Zip Code/Country**

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (Includes Reference to PCT International Applications)				Attorney's Docket Number. 6028.200-US
5	Full Name of Inventor	Family Name	First Given Name	Second Given Name
	Residence & Citizenship	City	State or Foreign Country	Country of Citizenship
	Post Office Address	Post Office Address	City	State & Zip Code/Country
6	Full Name of Inventor	Family Name	First Given Name	Second Given Name
	Residence & Citizenship	City	State or Foreign Country	Country of Citizenship
	Post Office Address	Post Office Address	City	State & Zip Code/Country
7	Full Name of Inventor	Family Name	First Given Name	Second Given Name
	Residence & Citizenship	City	State or Foreign Country	Country of Citizenship
	Post Office Address	Post Office Address	City	State & Zip Code/Country
8	Full Name of Inventor	Family Name	First Given Name	Second Given Name
	Residence & Citizenship	City	State or Foreign Country	Country of Citizenship
	Post Office Address	Post Office Address	City	State & Zip Code/Country
9	Full Name of Inventor	Family Name	First Given Name	Second Given Name
	Residence & Citizenship	City	State or Foreign Country	Country of Citizenship
	Post Office Address	Post Office Address	City	State & Zip Code/Country

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon

Signature of Inventor 1	Signature of Inventor 2	Signature of Inventor 3
Date	Date	Date
Signature of Inventor 4	Signature of Inventor 5	Signature of Inventor 6
Date	Date	Date
Signature of Inventor 7	Signature of Inventor 8	Signature of Inventor 9
Date	Date	Date